Dronabinol

Brand Name: Marinol

AIDSinfo
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Drug Description

Dronabinol is synthetic delta-9-tetrahydrocannabinol (delta-9-THC). Delta-9-THC is a naturally occurring component of Cannabis sativa L. (marijuana). [1]

HIV/AIDS-Related Uses

Dronabinol was approved by the FDA on December 23, 1992 for use in the treatment of anorexia associated with weight loss in patients with HIV/AIDS. Tachyphylaxis and tolerance to some effects of dronabinol develop with chronic use; unlike the cardiovascular and central nervous system (CNS) effects, the appetite stimulant effects of dronabinol have been sustained for up to 5 months in AIDS patients receiving doses ranging from 2.5 mg to 20 mg dronabinol daily.[2]

Non-HIV/AIDS-Related Uses

Dronabinol is indicated in selected patients for the prevention of nausea and vomiting associated with emetogenic cancer chemotherapy when other antiemetic medications are not effective.[3]

Pharmacology

The exact mechanism of action of dronabinol is not known. Cannabinoid receptors in neural tissue may mediate the effects of dronabinol and other cannabinoids. Animal studies with other cannabinoids suggest that dronabinol's antiemetic effects may be due to inhibition of the vomiting control mechanism in the medulla oblongata. Central sympathomimetic activity may result in tachycardia and/or conjunctival injection. Dose-related reversible effects on appetite, mood, cognition, memory, and perception also occur, subject to great interpatient variability.[4]

Although dronabinol is 90% to 95% absorbed after administration of single oral doses, only 10% to 20% reaches systemic circulation due to first-pass hepatic metabolism and high lipid solubility. Peak concentration is reached 2 to 4 hours after oral administration. Dronabinol and its active metabolite, 11-OH-delta-9-THC, are present in approximately equal concentrations in plasma.[5] Psychoactive effects last 4-6 hours; appetite stimulating effects last 24 hours or longer.[6] Apparent volume of distribution is approximately 10 L/kg.[7]

Dronabinol is in FDA Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women. Reproduction studies in mice [at doses 0.2 times to 5 times the maximum recommended human dose (MRHD) in cancer patients and 1 time to 30 times the MRHD in AIDS patients] and in rats (at doses 0.8 times to 3 times the MRHD in cancer patients and 5 times to 20 times the MRHD in AIDS patients) have revealed no evidence of teratogenicity. However, increased fetal mortality, early resorptions, and dose-dependent effects, including decreased weight gain and number of viable pups, were observed.[8] Dronabinol is distributed into human breast milk.[9]

Dronabinol binds very highly (97%) to protein. Dronabinol is eliminated in a biphasic manner, with an alpha (first) half-life of 4 hours and a beta (terminal) phase of 25 to 36 hours. First-pass hepatic metabolism, primarily by microsomal hydroxylation, yields both active and inactive metabolites.[10]

Elimination is primarily fecal (biliary), with approximately 50% of an oral dose appearing in the feces (less than 5% as unchanged drug) and 10% to 15% in the urine (as unchanged drug or as metabolite) within 72 hours.[11] Following single dose administration, low levels of dronabinol metabolites have been detected for more than 5 weeks in the urine and feces.[12]

Adverse Events/Toxicity

Adverse effects observed with use of dronabinol include CNS effects, heart palpitations, tachycardia, ataxia, dizziness, drowsiness, euphoria, nausea, trouble thinking, vomiting, asthenia, blurred vision or other changes in vision, dryness of mouth, vasodilation and flushing of face, orthostatic hypotension (lightheadedness), and restlessness.[13]

Dronabinol

Drug and Food Interactions

Concurrent use of dronabinol with alcohol, CNS depression-producing medications, or apomorphine may potentiate the CNS-depressant effects of either dronabinol or these medications. Prior administration of dronabinol may decrease the emetic response to apomorphine. Anticholinergics, antihistamines, and CNS stimulation-producing medications (especially amphetamines, cocaine, and sympathomimetic agents) may cause additive or super-additive tachycardia and possible cardiotoxicity if used concurrently with dronabinol.[14]

Because dronabinol is highly protein bound to plasma proteins, it might displace other protein-bound drugs. Although this displacement has not been confirmed in vivo, practitioners should monitor patients for a change in dosage requirements when administering dronabinol to patients receiving other highly protein-bound drugs.[15]

Contraindications

Dronabinol is contraindicated in any patient with known hypersensitivity to any known cannabinoid or to sesame oil. The risk/benefit ratio of dronabinol use should be carefully evaluated in patients with cardiac disorders caused by occasional hypotension, possible hypertension, syncope, or tachycardia; a history of substance abuse (including acute alcoholism); psychosis, bipolar disorder, mania, depression, or schizophrenia; and those requiring concomitant therapy with sedatives, hypnotics, or other psychoactive drugs. Dronabinol should be prescribed to pregnant women, nursing mothers, and pediatric patients with caution; the drug has not been studied in these patient populations. Patients with any of these conditions should be carefully monitored by their physicians because of individual variation in response and tolerance to the effects of dronabinol.[16] [17]

Clinical Trials

For information on clinical trials that involve Dronabinol, visit the ClinicalTrials.gov web site at http://www.clinicaltrials.gov. In the Search box, enter: Dronabinol AND HIV Infections.

Dosing Information

Mode of Delivery: Oral.[18]

Dosage Form: Dronabinol capsules containing 2.5 mg, 5 mg, and 10 mg dronabinol in sesame oil.[19]

Storage: Dronabinol capsules should be packaged in a well-closed container and stored between 8 C and 15 C (46 F and 59 F). Alternatively, dronabinol can be stored in a refrigerator, but it should be protected from freezing.[20]

Chemistry

CAS Name:
1-trans-delta9-Tetrahydrocannabinol[21]

CAS Number: 1972-08-3[22]

Molecular formula: C21-H30-O2[23]

C80.21%, H9.62%, O10.18%[24]

Molecular weight: 314.46[25]

Boiling point: 200 C[26]

Physical Description: Dronabinol is a light-yellow, resinous oil that is sticky at room temperature and hardens upon refrigeration.[27]

Solubility: Dronabinol is insoluble in water and is formulated in sesame oil.[28]

Other Names

Marijuana[29]

Tetrahydrocannabinol[30]

THC[31]

delta9-THC[32]

9-ene-Tetrahydrocannabinol[33]

Dronabinol

Further Reading

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Manufacturer Information

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For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

• Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET

• Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

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